REMARKS

Claims 1-2, 4, 7-9, 14-26, 33-45 and 48-56 were pending in the application. Claims 8 and 49-56 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-2, 4, 7, 9, 14-16, 24-26, 33-37 and 45 have been amended. Accordingly, upon entry of the amendments presented herein, claims 1-2, 4, 7-9, 14-26, 33-45 and 48-56 will be pending in the application.

No new matter has been added. Support for the amendments to the claims can be found in the claims and throughout the specification as originally filed. In particular, support for the amendments to claims 1, 2, 4, 7 and 9 to recite "altered activity or expression of a cholinergic pathway molecule" can be found at least at page 11, lines 17-20 and lines 25-30, and at page 12, lines 1-5 of the specification. Support for the amendment to claims 14, 15 and 24-26 to recite "wherein the indicator of said cholinergic pathway is selected from the group consisting of muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13, or a mammalian orthologue thereof" can be found at least at page 22, lines 22-24, page 23, lines 26-29, page 25, lines 19-21 and page 26, lines 3-5. Support for the amendment to claim 45 to recite "wherein said assay composition comprises a cholinergic pathway molecule selected from the group consisting of EGL-30, EGL-3 and RIC-8, or a mammalian orthologue of said cholinergic pathway molecule" can be found at least at page 29, lines 24-26. Support the amendment to claim 45 to recite "*cell-free* assay composition" can be found at least at page 29, lines 18-29 and page 30, lines 7-8.

Amendments to and cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and were done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

Rejection of Claims 1-2, 4, 7 and 9 Under 35 U.S.C. 112, Second Paragraph

The Examiner has rejected claims 1-2, 4, 7 and 9 under 35 U.S.C. 112, second paragraph as being indefinite for recitation of "deregulated cholinergic pathway" and

"increased lifespan is associated with said deregulated cholinergic pathway." Specifically, the Examiner alleges that it is unclear whether this phrase means that "certain molecules within the pathway are mutated... that the pathway is constitutively active or silent" or "that a neuron which comprises this pathway is firing at a rate different from the average." The Examiner indicates that "[i]f applicant is attempting to claim methods of using nematodes with genetic mutations in certain specific molecules, reciting these in the claims might be sufficient to overcome this ambiguity." The Examiner further alleges that recitation of the term "is associated with" is unclear. Specifically, the Examiner contends that this phrase "could mean that the specific change or mutation in the pathway leads to an increase in longevity, or it could mean that there is a negative correlation between the change and longevity."

Applicants respectfully traverse the Examiner's rejection on the grounds that the claims are clear and definite. Claim 1 (and claims 4, 7 and 9, which depend therefrom) has been amended so that it is now directed to a method for identifying an agent capable of enhancing longevity, comprising contacting an organism having ***altered activity or expression of at least one cholinergic pathway molecule*** with a test agent, wherein said ***altered activity or expression of the at least one cholinergic pathway molecule leads to increased lifespan.*** Similarly, claim 2 (and claims 4, 7 and 9, which depend therefrom) has been amended so that it now recites "wherein said organism further has ***altered activity or expression of at least one insulin signaling pathway molecule***, wherein said ***altered activity or expression of the at least one deregulated cholinergic pathway molecule or said altered activity or expression of the at least one insulin signaling pathway molecule leads to increased lifespan***. Applicants submit that, in view of the amendments to the claims, one of skill in the art would understand the metes and bounds of the claimed invention.

In view of the foregoing, Applicants submit that claims 1, 2, 4, 7 and 9 are clear and definite, and respectfully request that the rejection of these claims as being indefinite be reconsidered and withdrawn.

Rejection of Claims 14-19, 21-22, 24-26, 33-36 and 40-45 Under 35 U.S.C. § 102(b)

The Examiner has maintained the rejection of claims 14-19, 21-22, 24-26, 33-36 and 40-45 under 35 U.S.C. § 102(b) as being anticipated by Ruvkun (U.S. Patent Application No. 2001/0029617). The Examiner relies on Ruvkun for teaching "contacting organisms with test agents, assaying for the ability of the agent to affect an indicator of the pathway, and identifying said agents as longevity-enhancers." The Examiner acknowledges that "paragraphs [0443]-[0445], drawn to screens for isolating longevity therapeutics... specifically discusses the insulin signaling pathway but does not explicitly mention the cholinergic pathway." The Examiner continues:

> [h]owever, at paragraphs [0162]-[0163] and Figure 46, Ruvkun clearly indicates that the insulin signaling pathway is immediately downstream of the cholinergic pathway. That is, the insulin signaling pathway is itself part of the cholinergic pathway, as binding of acetylcholine to the cholinergic receptor causes insulin release... and of course subsequent activation of the insulin pathway. A "pathway" does not have a specific definition in the art, but is understood to be a series of molecules which are all involved in a common function.... By measuring outputs and indicators of the insulin signaling pathway, Ruvkun is also measuring outputs of the cholinergic pathway, as acetylcholine signaling activates insulin signaling."

Based on the foregoing, the Examiner concludes that Ruvkun anticipates the pending claims.

Applicants respectfully traverse this rejection on the grounds that Ruvkun fails to teach or suggest each and every element of the claimed invention in accordance with 35 U.S.C. §102(b). For a prior art reference to anticipate a claimed invention under 35 U.S.C. 102, the prior art must teach *each and every element* of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

The claims, as currently amended, are directed to a method for identifying an agent capable of enhancing longevity, involving contacting an organism or a cell with a test agent, said organism or cell having a cholinergic pathway, assaying for the ability of the test agent to inhibit the cholinergic pathway by monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an indicator of said cholinergic pathway as compared to a suitable control, wherein the ***indicator of said cholinergic pathway is selected from the group***

consisting of muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13, or a mammalian orthologue thereof, and selecting an agent that inhibits the cholinergic pathway, to thereby identify an agent capable of enhancing longevity.

The claims, as currently amended, are further directed to a method for identifying an agent capable of enhancing longevity, comprising contacting an organism or a cell with a test agent, said organism or cell having a cholinergic pathway and an insulin signaling pathway, assaying for the ability of the test agent to inhibit the cholinergic pathway and insulin signaling pathway by: (i) monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of at least one indicator of said cholinergic pathway, wherein the ***indicator of said cholinergic pathway is selected from the group consisting of muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13, or a mammalian orthologue thereof***, and (ii) monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization, or synaptic release of at least one indicator of said insulin signaling pathway, and selecting an agent that inhibits the cholinergic pathway and insulin signaling pathway, to thereby identify an agent capable of enhancing longevity.

The claims, as currently amended, are further directed to a method for identifying an agent capable of enhancing longevity, comprising contacting a ***cell-free*** assay composition with a test agent in vitro, wherein said cell-free assay composition comprises a ***cholinergic pathway molecule selected from the group consisting of EGL-30, EGL-3 and RIC-8, or a mammalian orthologue of said cholinergic pathway molecule***, assaying for the ability of the test agent to affect the activity or expression of said cholinergic pathway molecule, and selecting an agent that inhibits the activity or expression of said cholinergic pathway molecule, to thereby identify an agent capable of enhancing longevity.

The teachings of Ruvkun with respect to screening assays for identifying agents that are useful in extending lifespan are limited to the identification of agents that ***modulate the insulin signaling pathway*** (see, *e.g.*, paragraphs 0443-0445) by monitoring the activity or phosphorylation of an ***insulin signaling pathway molecule***. The teachings of Ruvkun related to the cholinergic pathway are limited to experiments involving contacting *C. elegans* with a known agonist of the muscarinic receptor and monitoring the single readout of dauer formation. The reference does not teach screening assays for the identification of ***inhibitors of the***

cholinergic pathway. In particular, Ruvkun fails to teach or suggest assaying the ability of an agent to inhibit the cholinergic pathway by ***monitoring the effect of the test agent on*** one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an ***indicator of the cholinergic pathway, wherein the indicator of said cholinergic pathway is selected from the group consisting of muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13,*** or a mammalian orthologue thereof, as required by the pending claims. Moreover, Ruvkun teaches the administration of ***known agonists*** of muscarinic receptors and the effects of those agents on dauer recovery. Ruvkun fails to teach or suggest the ***selection*** of an agent based on the ability to ***inhibit*** the cholinergic pathway or the activity or expression of a cholinergic pathway molecule, as required by the pending claims. Moreover, Ruvkun fails to teach or suggest a method of contacting a ***cell-free assay composition*** comprising *any* cholinergic pathway molecule with a test agent *in vitro*, let alone a cholinergic pathway molecule selected from the group consisting of EGL-30, EGL-3 and RIC-8, or a mammalian orthologue of said cholinergic pathway molecule, as required by claim 45.

In summary, it is evident that Ruvkun fails to teach each and every element of the claims, and therefore, fails to anticipate the claimed invention. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102(b) over Ruvkun be reconsidered and withdrawn.

Rejection of Claims 14, 16-17, 19, 24, 33-34, 36 and 38-39 Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 14, 16-17, 19, 24, 33-34, 36 and 38-39 under 35 U.S.C. § 102(b) as being anticipated by Pasricha (1994 Gut 35:1319-1321). The Examiner relies on Pasricha for teaching "methods of administering botulinum toxin, which prevents acetylcholine release and therefore is 'an agent that inhibits the cholinergic pathway,' to human patients." The Examiner further relies on Pasricha for teaching "assaying for the ability of the agent... to inhibit the cholinergic pathway by monitoring the activity of an indicator," where the ***indicator is "sphincter of Oddi pressure... biliary scintigraph... and perceived pain"*** (emphasis added). The Examiner alleges that Pasricha's conclusion that "'intrasphincteric botulinum toxin injection seems to lower sphincter of Oddi pressure'... reasonably constitutes

selecting the agent." Finally, the Examiner states that "[w]hile the reference does not explicitly discuss identifying the agents as being capable of enhancing longevity, such a step is not explicitly required by independent claims 14... and 24" and concludes that "as the prior art teaches every active step of claims 14 and 24, the reference anticipates the claimed invention."

Applicants respectfully traverse this rejection on the grounds that Pasricha fails to teach or suggest each and every element of the claimed invention in accordance with 35 U.S.C. §102(b). For a prior art reference to anticipate a claimed invention under 35 U.S.C. 102, the prior art must teach *each and every element* of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

The claims, as currently amended, are directed to a method for identifying an agent capable of enhancing longevity, comprising contacting an organism or a cell with a test agent, said organism or cell having a cholinergic pathway, assaying for the ability of the test agent to inhibit the cholinergic pathway by monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an indicator of said cholinergic pathway as compared to a suitable control, wherein the ***indicator of said cholinergic pathway is selected from the group consisting of muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13, or a mammalian orthologue thereof***, and selecting an agent that inhibits the cholinergic pathway, to thereby identify an agent capable of enhancing longevity.

The claims, as currently amended, are further directed to a method for identifying an agent capable of enhancing longevity, comprising contacting an organism or a cell with a test agent, said organism or cell having a cholinergic pathway and an insulin signaling pathway, assaying for the ability of the test agent to inhibit the cholinergic pathway and insulin signaling pathway by: (i) monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of at least one indicator of said cholinergic pathway, wherein the ***indicator of said cholinergic pathway is selected from the group consisting of muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13, or a mammalian orthologue thereof***, and (ii) monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction, cellular localization, or synaptic release of at least one indicator of said insulin signaling

pathway, and selecting an agent that inhibits the cholinergic pathway and insulin signaling pathway, to thereby identify an agent capable of enhancing longevity.

Pasricha teach administering botulinum toxin to human patients and monitoring the indicators of ***sphincter of Oddi pressure, biliary scintigraph and perceived pain***. Dunant fail to teach or suggest assaying for the ability of a test agent to inhibit the cholinergic pathway by monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an indicator of said cholinergic pathway as compared to a suitable control, wherein the indicator of said cholinergic pathway is selected from the group consisting of ***muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13***, or a mammalian orthologue thereof, as required by the pending claims.

In view of the foregoing, it is evident that Pasricha fails to teach each and every element of the claims, and therefore, fails to anticipate the claimed invention. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102(b) over Pasricha be reconsidered and withdrawn.

Rejection of Claims 14, 24 and 45 Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 14, 24 and 45 under 35 U.S.C. § 102(b) as being anticipated by Dunant (1990 J. Physiol. Paris 84:211-219). The Examiner relies on Dunant for teaching methods of administering botulinum toxin... to fish and to cells taken from fish" and for teaching that "large doses of botulinum toxin (5 x 106 MLD) injected into Torpedo electric organ decreases the reflex electrical discharge from 65 V to 44 V." The Examiner further relies on Dunant for teaching "contacting cells (contained in prisms) from Torpedo electric organs with botulinum toxin and measuring the effect on voltage... measuring the degree of synaptic release of acetylcholine" and "selecting the botulinum toxin for further experimentation." The Examiner alleges that Dunant anticipates claim 45 since "the prisms isolated from Torpedo electric organs are reasonably 'an assay composition' which are contacted with the test agent botulinum toxin *in vitro*." Finally, the Examiner states that "the final step recited in [the claims] ("to thereby identify an agent") does not actually require additional steps and therefore can reasonably be construed as an intended use of the method." The Examiner concludes, based on the foregoing, that Dunant anticipates the claimed invention.

Applicants respectfully traverse this rejection on the grounds that Dunant fails to teach or suggest each and every element of the claimed invention in accordance with 35 U.S.C. §102(b). For a prior art reference to anticipate a claimed invention under 35 U.S.C. 102, the prior art must teach *each and every element* of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

Claims 14 and 24, as currently amended, are directed to a method for identifying an agent capable of enhancing longevity, comprising contacting an organism or a cell, respectively, with a test agent, said organism or cell having a cholinergic pathway, assaying for the ability of the test agent to inhibit the cholinergic pathway by monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an indicator of said cholinergic pathway as compared to a suitable control, wherein the ***indicator of said cholinergic pathway is selected from the group consisting of muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13, or a mammalian orthologue thereof***, and selecting an agent that inhibits the cholinergic pathway, to thereby identify an agent capable of enhancing longevity.

Claim 45, as currently amended, is directed to a method for identifying an agent capable of enhancing longevity, comprising contacting a ***cell-free assay composition*** with a test agent in vitro, wherein said cell-free assay composition comprises a cholinergic pathway molecule selected from the group consisting of EGL-30, EGL-3 and RIC-8, or a mammalian orthologue of said cholinergic pathway molecule, assaying for the ability of the test agent to affect the activity or expression of said cholinergic pathway molecule, and selecting an agent that inhibits the activity or expression of said cholinergic pathway molecule, to thereby identify an agent capable of enhancing longevity.

Dunant teach the administration of botulinum toxin to fish or fish cells, and subsequently monitoring the effect of the toxin on ***voltage*** or the ***degree of synaptic release of acetylcholine***. Dunant fail to teach or suggest assaying for the ability of a test agent to inhibit the cholinergic pathway by monitoring the effect of the test agent on one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an indicator of said cholinergic pathway as compared to a suitable control, wherein the indicator of said cholinergic pathway is selected from the group consisting of ***muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13***, or a mammalian orthologue thereof, as required by claims 14 and 24. Moreover, Dunant fails to

teach or suggest a ***cell-free assay composition*** comprising *any* cholinergic pathway molecule, let alone a cholinergic pathway molecule selected from the group consisting of EGL-30, EGL-3 and RIC-8, or a mammalian orthologue of said cholinergic pathway molecule, as required by claim 45.

In view of the foregoing, it is evident that Dunant fails to teach each and every element of the claims, and therefore, fails to anticipate the claimed invention. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102(b) over Dunant be reconsidered and withdrawn.

Rejection of Claims 45 and 48 Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 45 and 48 under 35 U.S.C. § 102(b) as being anticipated by Richardson (1991 Molecular Pharmacology 40:908-914). The Examiner relies on Richardson for teaching cell-free assay compositions "comprising purified muscarinic receptors," "assays to determine binding of ligand to the receptors" and "selecting agents (i.e., antibodies) which inhibit the activity (G-protein signaling) of the receptor." The Examiner alleges that "the final step recited in claim 45 does not actually require additional steps and therefore can reasonably be construed as an intended use of the method." The Examiner concludes, based on the foregoing, that Richardson anticipates the claimed invention.

Applicants respectfully traverse this rejection on the grounds that Richardson fails to teach or suggest each and every element of the claimed invention in accordance with 35 U.S.C. §102(b). For a prior art reference to anticipate a claimed invention under 35 U.S.C. 102, the prior art must teach *each and every element* of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

Claims 45 and 48, as currently amended, are directed to a method for identifying an agent capable of enhancing longevity, comprising contacting a cell-free assay composition with a test agent in vitro, wherein said cell-free assay composition comprises a cholinergic pathway molecule selected from the group consisting of ***EGL-30, EGL-3 and RIC-8***, or a mammalian orthologue of said cholinergic pathway molecule, assaying for the ability of the test agent to affect the activity or expression of said cholinergic pathway molecule, and selecting an agent that inhibits the activity or expression of said cholinergic pathway molecule, to thereby identify an agent capable of enhancing longevity.

In contrast, the teachings of Richardson are limited to cell-free assay compositions comprising purified muscarinic receptor. Richardson fails to teach or suggest a cell-free assay composition comprising a cholinergic pathway molecule selected from the group consisting of ***EGL-30, EGL-3 and RIC-8***, or a mammalian orthologue of said cholinergic pathway molecule. Richardson also fails to teach or suggest assaying for the ability of a test agent to affect the activity or expression of a cholinergic pathway molecule selected from the group consisting of ***EGL-30, EGL-3 and RIC-8***, or a mammalian orthologue of said cholinergic pathway molecule, let alone selecting an agent that inhibits the activity or expression of said cholinergic pathway molecule, as required by the claims.

In view of the foregoing, it is evident that Richardson fails to teach each and every element of the claims, and therefore, fails to anticipate the claimed invention. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102(b) over Richardson be reconsidered and withdrawn.

Rejection of Claims 14-19, 21-26, 33-36, 40-43 and 45
Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 14-19, 21-26, 33-36, 40-43 and 45 under 35 U.S.C. § 103(a) as being obvious over Ruvkun. The Examiner relies on Ruvkun for the reasons discussed above. The Examiner acknowledges that "Ruvkun does not explicitly teach performing the screening assay [for identifying agents which *enhance longevity*] encompassed by claims 14 and 15, in a parasitic nematode such as *A. caninum*." The Examiner contends that "it would have been obvious to one of ordinary skill in the art to perform the screening assays... from Ruvkun on parasitic nematodes, with a reasonable expectation of success... [since] Ruvkun

teaches that the biochemical pathways found in *C. elegans* are also present in the parasitic nematode." The Examiner concludes, based on the foregoing, that "the invention of claim 23 is obvious."

Applicants respectfully traverse this rejection on the grounds that the claimed methods would not have been obvious to one of ordinary skill in the art based on the teachings of Ruvkun.

The test for *prima facie* obviousness is consistent with the legal principles enunciated in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). *Takeda Chem. Indus., Ltd. v. Alpharma Pty., Ltd.*, 2007 U.S. App. LEXIS 15349, at *13 (Fed. Cir. 2007). "While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test, the Court acknowledged the importance of identifying 'a *reason* that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination." *Id.* at *13-14 (quoting *KSR,* 127 S. Ct. at 1731) (emphasis added). Although the TSM test should not be applied in a rigid manner, it can provide helpful insight to an obviousness inquiry. *KSR,* 127 S. Ct. at 1731. The *KSR* Court upheld the secondary considerations of non-obviounsess, noting that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." *Id.*

As discussed above with respect to the rejection of claims 14-19, 21-26, 33-36, 40-43 and 45 under 35 U.S.C. 102(b), the teachings of Ruvkun related to the cholinergic pathway are limited to experiments involving contacting *C. elegans* with an agonist of the muscarinic receptor and monitoring the single readout of dauer formation. Ruvkun fails to teach or suggest assaying the ability of an agent to inhibit the cholinergic pathway by ***monitoring the effect of the test agent on*** one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an ***indicator of the cholinergic pathway, wherein the indicator of said cholinergic pathway is selected from the group consisting of muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13,*** or a mammalian orthologue thereof, as required by the pending claims. Moreover, Ruvkun teaches the administration of ***known agonists*** of muscarinic receptors and the effects of those agents on dauer recovery. Ruvkun fails to teach or suggest the ***selection*** of an agent based on the ability to ***inhibit*** the cholinergic pathway or the activity or expression of a cholinergic pathway molecule, as required by the pending claims. Moreover, Ruvkun fails to teach or

suggest a method of contacting a ***cell-free assay composition*** comprising *any* cholinergic pathway molecule with a test agent *in vitro*, let alone a cholinergic pathway molecule selected from the group consisting of EGL-30, EGL-3 and RIC-8, or a mammalian orthologue of said cholinergic pathway molecule, as required by claims 45 and 48. In view of the foregoing, the claimed screening assays, including assays carried out in parasitic nematodes, would not be obvious based on the teachings of Ruvkun.

Moreover, one of skill in the art would not have had a reasonable expectation of success, based on the disclosure of Ruvkun, to arrive at the claimed invention. As indicated above, the teachings of Ruvkun related to the cholinergic pathway are limited to experiments involving contacting *C. elegans* with an agonist of the muscarinic receptor and monitoring the ***single readout of dauer formation***. Dauer formation and enhanced life span are completely different phenotypes. Absent the teachings of the present invention which clearly link the inhibition of the cholinergic pathway with ***increased life span***, there would have been no reasonable expectation of success in identifying agents that increase longevity using the presently claimed assays.

In summary, Applicants respectfully submit that, in view of the foregoing, it is evident that Ruvkun fails to render the claimed invention obvious. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. 103(a) be reconsidered and withdrawn.

Rejection of Claims 14-19, 21-26, 33-36, 40-43 and 45
Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 14-22, 24-26, 33-37, 40-43 and 45 under 35 U.S.C. § 103(a) as being obvious over Ruvkun. The Examiner relies on Ruvkun for the reasons discussed above. The Examiner acknowledges that Ruvkun "does not explicitly teach monitor[ing] the ability of agents to alter cellular localization of indicators, as recited in claims 20 and 37, while performing the screening assays set forth in independent claims 14-15 or 24-26." The Examiner contends that "it would have been obvious to one of ordinary skill in the art to monitor cellular localization of indicators when performing the assays taught in Ruvkun ... [since Ruvkun] teaches that monitoring cellular localization is useful in identifying targets for diabetes, which is related to the insulin signaling pathways."

Applicants respectfully traverse this rejection on the grounds that the claimed methods would not have been obvious to one of ordinary skill in the art based on the teachings of Ruvkun.

As discussed above with respect to the rejection of claims 14-19, 21-26, 33-36, 40-43 and 45 under 35 U.S.C. 102(b), the teachings of Ruvkun related to the cholinergic pathway are limited to experiments involving contacting *C. elegans* with an agonist of the muscarinic receptor and monitoring the single readout of dauer formation. Ruvkun fails to teach or suggest assaying the ability of an agent to inhibit the cholinergic pathway by ***monitoring the effect of the test agent on*** one or more of the expression, intracellular level, extracellular level, activity, post-translational modification, interaction or cellular localization of an ***indicator of the cholinergic pathway, wherein the indicator of said cholinergic pathway is selected from the group consisting of muscarinic receptor, EGL-30, EGL-8, RIC-8, DAG, SNARE complex and UNC-13,*** or a mammalian orthologue thereof, as required by the pending claims. Moreover, Ruvkun teaches the administration of ***known agonists*** of muscarinic receptors and the effects of those agents on dauer recovery. Ruvkun fails to teach or suggest the ***selection*** of an agent based on the ability to ***inhibit*** the cholinergic pathway or the activity or expression of a cholinergic pathway molecule, as required by the pending claims. Moreover, Ruvkun fails to teach or suggest a method of contacting a ***cell-free assay composition*** comprising *any* cholinergic pathway molecule with a test agent *in vitro*, let alone a cholinergic pathway molecule selected from the group consisting of EGL-30, EGL-3 and RIC-8, or a mammalian orthologue of said cholinergic pathway molecule, as required by claim 45. It follows, therefore, that the claimed screening assays involving monitoring the ability of agents to alter cellular localization of the recited indicators of the cholinergic pathway, as required by the pending claims, would not be obvious based on the teachings of Ruvkun.

In view of the foregoing, it is evident that Ruvkun fails to render the claimed invention obvious. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. 103(a) be reconsidered and withdrawn.

CONCLUSION

Applicant believes no additional fees are due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. UMY-035RCE from which the undersigned is authorized to draw.

Dated: **September 8, 2008**

Respectfully submitted,

By_____

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